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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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09/430,029	10/29/1999	TETSUYA YANO	35.C13982	6685
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EXAMINER

SLOBODYANSKY, ELIZABETH

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 08/13/2002

22

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/430,029

Applicant(s)

YANO ET AL.

Examiner

Elizabeth Slobodyansky

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 08 April 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-48 and 55 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 2, 15 and 16 is/are allowed.
- 6) ☒ Claim(s) 3-14, 17-48 and 55 is/are rejected.
- 7) ☒ Claim(s) 1 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

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DETAILED ACTION

Continued Prosecution Application

The request filed on April 8, 2002 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/430,029 is acceptable and a CPA has been established. An action on the CPA follows.

The Notice Re deposit of microorganisms filed December 18, 2001 signed by Mr. Peter Saxon has been entered.

The AF amendment filed December 18, 2001 amending claims 2-4, 9-11, 15, 17 and 55 has been entered.

The AF amendment filed February 26, 2002 amending claims 9, 10 and 55 has been entered.

Claims 1-48 and 55 are pending.

Claim Objections

Claims 1 and 8 are objected to because of the following informalities:

In claim 1, the name "Burkholderia" appears to be mistyped.

In claim 8, the reference to "in the Sequence listing" is not necessary.

Appropriate correction is required.

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Claim 13 is objected to under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim should refer to other claims in the alternative only and cannot depend from any other multiple dependent claim. See MPEP § 608.01(n).

For the sake of expedient prosecution, the examiner interprets the claim as the set of claims dependent from an individual claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 3-5, 9-14, 17, 18, 21-48 and 55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 3 and 10 are drawn to a DNA fragment that hybridizes under stringent conditions to SEQ ID NO:1 or a portion thereof from nucleotide 234 to 443, respectively. The claims are not limited by function. The stringent conditions are not defined.

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The specification does not contain any disclosure of the function of all DNA sequences that hybridize to SEQ ID NO:1 or its 234-443 portion. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many functionally unrelated DNAs, both naturally occurring and man made, including partial DNA sequences, are encompassed within the scope of these claims. The specification discloses only a single species of the claimed genus, SEQ ID NO:1 and the 234-443 portion thereof, and fails to provide any structure: function correlation present in all members of the claimed genus, which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. One skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 9 and 17 are drawn to a DNA fragment encoding a toluene monooxygenase that hybridizes under stringent conditions to SEQ ID NO:1 or portions thereof. Claim 13 and 55 recite a DNA fragment encoding TomK that hybridizes under stringent conditions to nucleotides 234-443 of SEQ ID NO:1. This is equivalent to claims with no structural limitations wherein an enzyme is defined by the function only. The specification discloses no identifying characteristics which would allow to recognize a structure as a member of a genus of a DNA encoding a toluene

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monooxygenase activity or TomK. Therefore, based on the instant disclosure, it is unpredictable either a DNA encodes a toluene monooxygenase or TomK.

The specification does not contain any disclosure of the structure and function of all DNA sequences that encode a toluene monooxygenase or portions thereof. The genus of DNAs that comprise these above DNA molecules is a large variable genus with the potentiality of encoding many different proteins. Therefore, many structurally and functionally unrelated DNAs are encompassed within the scope of these claims, including partial DNA sequences. The specification discloses only a single species of the claimed genus. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties other than the "functionality" of encoding a toluene monooxygenase or TomK and fails to provide any structure: function correlation present in all members of the claimed genus. Therefore, the specification is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims not specifically rejected in the above rejection, are rejected as dependent from the rejected base claim.

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Claims 3-5 and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a DNA fragment that hybridizes under stringent conditions to SEQ ID NO:1 or a portion thereof from nucleotide 234 to 443 and encodes a toluene monooxygenase, does not reasonably provide enablement for said DNA encoding a polypeptide of an unknown function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, how to use the invention commensurate in scope with these claims.

As discussed above, the claim is directed to a DNA encoding a polypeptide of an undisclosed function. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of encoded polypeptides having toluene monooxygenase or TomK activity and lacking said functions but possibly exhibiting other undisclosed functions.

Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which structure would impart the desired activity requires a detailed knowledge of the ways in which the proteins' structure relates to its function and vice versa, in general, the state of the art does not allow the predictability of function based on a structure. However, in this case the disclosure lacks any information regarding the correlation between function and structure. Without knowing the function it is impossible to know how to use a DNA fragment.

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Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including a DNA fragment that hybridizes under stringent conditions to SEQ ID NO:1 or a portion thereof from nucleotide 234 to 443 and encodes a polypeptide of any undisclosed function. Without such guidance, the experimentation left to those skilled in the art is undue.

Claims 9, 11-14, 17, 18, 22-48 and 55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a toluene monooxygenase encoded by sequence of SEQ ID NO:1 and a DNA encoding TomK of 234-443 portion of SEQ ID NO: 1, does not reasonably provide enablement for a DNA encoding a toluene monooxygenase and TomK of an unknown amino acid sequence encoded by a DNA that hybridizes to said sequences. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be in In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the

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art, (7) considered in determining whether undue experimentation is required, are summarized the predictability or unpredictability of the art, and (8) the breadth of the claims.

The instant invention is directed to a gene encoding a toluene monooxygenase having the sequence of SEQ ID NO:1. The above claims are drawn to sequences having structures different from SEQ ID NO: 1 and the 234-443 portion thereof and encoding a polypeptide retaining the requisite function.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of a sequence that comprises SEQ ID NO:1 and its portion and encodes a toluene monooxygenase or TomK activity. This is because the specification does not establish: (a) regions of the protein structure which may be modified without effecting the specific requisite activity of the polypeptide of the instant invention; (B) the general tolerance of said polypeptide to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Despite knowledge in the art to produce mutations in proteins, the specification fails to provide guidance as to where, and what type of (i.e., what amino acid to substitute into, add to or delete from the known sequence), changes in amino acid

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residues will result in a desired enzymatic activity. The amino acid sequence of a protein determines its structural and functional properties, and predictability of what mutations can be tolerated in a protein's sequence and result in a certain activity is extremely complex, and well outside the realm of routine experimentation, because accurate predictions of a protein's function from mere sequence data are limited.

Furthermore, while recombinant and mutagenesis techniques are known, it is not routine in the art to screen large numbers of mutated proteins or genes where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Therefore, one of ordinary skill in the art would require guidance, in order to make a DNA fragment encoding a toluene monooxygenase or TomK having the sequence other than SEQ ID NO: 1 and its 234-443 portion, respectively, in a manner reasonably correlated with the scope of the claims. Without such guidance, the experimentation left to those skilled in the art is undue.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3, 5-14, 17-48 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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Claims 3, 9, 10, 13 and 17 recite "stringent hybridization conditions" rendering the metes and bounds of the claims unascertainable. Said conditions are not defined in the specification. Depending on the conditions nucleotide sequences of different structures would hybridize with the given sequence. Without knowing the exact conditions there is no way of knowing nucleotide sequences of what structure (homology) are encompassed by the scope of the claims.

Claim 5 is confusing because it recites "a recombinant DNA fragment according to claim 4" wherein claim 4 is drawn to "a recombinant DNA" but said DNA comprises a DNA fragment.

Claims 6, 9 and 19 recite a DNA fragment encoding "a toluene monooxygenase" but recite at the end of the claims "an active monooxygenase" rendering the claim confusing. Amending the claims to recite either "an active toluene monooxygenase", "said toluene monooxygenase", "the toluene monooxygenase", "said monooxygenase" or "the monooxygenase" would obviate this rejection.

Claim 13 uses a semicolon instead of a transitional term such as "comprising", for example. Further, a promoter does not express, but a vector can be an expression vector. The claim recites "the DNA fragment encoding polypeptide TomK according to claim 10" wherein claim 10 does not recite TomK.

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Claims 17 recites "the DNA fragment contains a toluene monooxygenase region of 4.9 kb or less". Amending the claim to "the DNA fragment of 4.9 kb or less encoding a toluene monooxygenase", for example, would obviate this rejection.

Claim 21 omits words connecting "transformant" and "produce". Amending the claim to "a method for producing a toluene monooxygenase comprising a step of culturing a transformant of claims 15, 17 or 19 in a medium and collecting the expressed toluene monooxygenase", for example, would obviate this rejection.

Claim 55 is confusing because it is unclear how the phrase "or a region that hybridizes ..." relates to the first or the second DNA fragment. Furthermore, a portion consisting of nucleotides from 463 to 1455 encodes TomL only.

Claims 27, 33 and 48 are confusing as reciting "the compound is at least one of" because the compound is one of.

Claim 34 is confusing as reciting "being at least either ... or". "at least" renders the scope unclear.

Claims not specifically rejected in the above rejection, are rejected as dependent from the rejected base claim.

Claims 22-48 provide for the use of the transformant, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it

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merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 22-48 are rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd. v. Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Response to Arguments

Applicant's arguments filed with the AF amendment filed February 26, 2002 have been responded to in the Advisory action mailed March 15, 2002. Applicants do not present further arguments.

Allowable Subject Matter

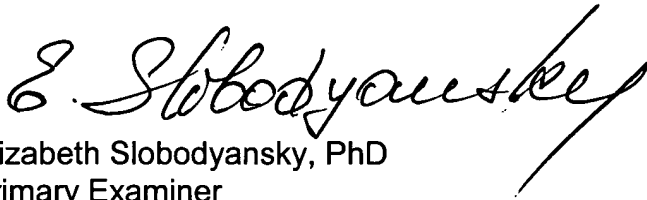
Claims 2, 15 and 16 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

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Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

A handwritten signature in black ink, reading "E. Slobodyansky". The signature is written in a cursive style with a long, sweeping underline that extends to the right.

Elizabeth Slobodyansky, PhD
Primary Examiner

August 9, 2002